

CLAIMS:

1. A method for the prevention of insulin dependent (type I) diabetes comprising administering to a prediabetic individual a composition comprising an anti-VLA-4 antibody.

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2. A method according to claim 1, wherein the anti-VLA-4 antibody selected from the group consisting of HPI/2, HP2/1, HP2/4, L25, and P4C2.

10 3. A method according to claim 1, wherein the anti-VLA-4 antibody is HPI/2, or a fragment thereof, capable of binding to VLA-4.

4. A method according to claim 1, wherein the anti-VLA-4 antibody is a humanized HPI/2 antibody, or a fragment thereof, capable of binding to VLA-4.

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5. A method according to claim 1, wherein the composition is administered at a dosage so as to provide from about 0.1 to about 10 mg/kg, based on the weight of the prediabetic individual.

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6. A method according to claim 1, wherein the composition is administered in an amount effective to coat VLA-4-positive cells in the peripheral blood for a period of 1-14 days.

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7. A method according to claim 1, wherein the composition is administered in an amount effective to provide a plasma level of antibody in the prediabetic individual of at least 1 µg/ml.

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8. A method according to claim 1, wherein the composition is administered prior to the development of overt diabetes, as measured by a serum glucose level of less than about 250 mg/dL.

9. A method according to claim 1, wherein the prediabetic individual is a human.

10. A method for the treatment of diabetes comprising administering to a mammal with a susceptibility to diabetes, an antibody, a recombinant antibody, a chimeric antibody, fragments of such antibodies, a polypeptide or a small molecule capable of binding to the  $\alpha_4$  subunit of VLA-4, or combinations of any of the foregoing, in an amount effective to provide inhibition of onset of diabetes.

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11. A method according to claim 10, wherein the antibody, polypeptide or molecule is selected from monoclonal antibody F(ab)2; Fab, Fab', F(ab')2 or F(v) fragments of such antibody; soluble VCAM-1 or fibronectin polypeptides; or small molecules that bind to the VCAM-1 or fibronectin binding domain of VLA-4.

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12. A method according to claim 11, wherein the soluble VCAM-1 polypeptides comprise a VCAM-IgG fusion.

10 13. A method according to claim 11, wherein the composition is administered in an amount effective to provide a plasma level of soluble VCAM-1 polypeptides in the mammal of at least 10-20 µg/ml over a period of 1-14 days.

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14. A method according to claim 11, wherein the soluble VCAM-1 polypeptides comprise VCAM 2D-IgG.

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A2 15. A method according to claim 10, wherein the composition comprises a plurality of anti-VLA-4 monoclonal antibodies or VLA-4-binding fragments thereof.

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16. A method according to claim 10, wherein the composition is administered at a dosage so as to provide from about 0.1 to about 10 mg/kg of antibody, antibody fragment, polypeptide or small molecule, based on the weight of the susceptible mammal.

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SAC 17. A method according to claim 10, wherein the composition is administered in an amount effective to coat VLA-4-positive cells in the peripheral blood for a period of 1-14 days.

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18. A method according to claim 10, wherein the composition is administered in an amount effective to provide a plasma level of antibody or antibody fragment in the mammal of at least 1 µg/ml over a period of 1-14 days.

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19. A method according to claim 10, wherein the composition is administered in an amount effective to provide a dosage of small molecule of about 0.1-10 mg/kg body weight/day over a period of 1-14 days.

20. A pharmaceutical composition effective to provide inhibition of onset of diabetes consisting essentially of a monoclonal antibody recognizing VLA-4 in a pharmaceutically acceptable carrier.

48 21. A chimeric molecule comprising:

a VLA-4 targeting moiety capable of binding to VLA-4 antigen on the surface of VLA-4 bearing cells and a toxin moiety.

22. The molecule of claim 21, wherein the VLA-4 targeting moiety comprises a  
5 portion of VCAM.

23. A method of treating a subject at risk for a disorder characterized by the presence of activated VLA-4 comprising administering to the subject the chimeric molecule of claims 21.

10 24. The method of claim 23, wherein said disorder is diabetes.

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